



<110> H. Robert Horvitz

SEQUENCE LISTING

<120> A TUMOR SUPPRESSOR PATHWAY IN C. ELEGANS

<130> 01997/202002

<140> 09/087,136

<141> 1998-05-28

<150> 60/047,996

<151> 1997-05-28

<160> 18

<170> FastSEQ for Windows Version 4.0

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<211> 275

<212> PRT

<213> Caenorhabditis elegans

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35 40 45
Pro Thr Val Pro Glu Ser Pro Asp Met Lys Phe Ala Arg Lys Arg Leu
50 55 60
Gly Asn Leu Leu Thr Thr Ile Lys His His Pro Ser Glu Ile Ile Gly
65 70 75 80
Val Leu Pro Glu Asp Tyr Thr Arg Ala Asp Glu Glu Pro Gly Arg Gln
85 90 95
Gly Arg Pro Pro Gly Arg Pro Arg Lys Met Pro Arg His Glu Ser Ser
100 105 110
Thr Ser Leu Met Glu Ser Pro Arg Lys Thr Met Thr Arg Asp Ser Lys
115 120 125
Ile Met Phe Glu Leu Arg Gly Lys Pro Phe Glu Met Ile Ala Gly Arg
130 135 140
Phe Glu Glu Glu Tyr Ser Leu Gly Arg Ala Trp Val Lys Gly His Met
145 150 155 160
Asn Asn Glu Tyr Glu Pro Ile Lys Ala Gln Arg Thr Asp Tyr Ala Pro
165 170 175
Asn Leu Ala Val Asp Tyr Leu Ala Cys Arg Glu Ile His Arg Met Pro
180 185 190
Arg Pro Asp Lys Ser Ile Pro Glu Leu Pro Ile Val Pro Ser Arg Ile

195 200 205
 Asp Glu Phe Asp Ala Thr Val Asp Pro Arg Tyr Glu Thr Asp Leu Lys
 210 215 220
 Asn Glu Tyr Ile Arg His Trp Lys Gln Val Lys Lys Gly Trp Cys Ala
 225 230 235 240
 His Gln Arg Arg Arg Thr Ala Pro His Ala Arg Ser Ile Ala Leu Ile
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 Asn Lys Ile Tyr Gln Pro Gly Glu Ser Lys Thr Val Glu Gln Ala Leu
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 Gly Leu Ile
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 <213> Caenorhabditis elegans

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 aagactatgat ctcgtgatttcaaaaattatg tttgaattgc gtggaaaacc attcgaaatg 360
 atagctggac gttttgaaga agaatattca cttggtagag catgggttaa aggacacatg 420
 aataatgaat atgaaccaat aaaagctcaa aggacagact atgcaccgaa tctggctgtt 480
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A7
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 <213> Caenorhabditis elegans

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 35 40 45
 Ile Lys Gln Glu Phe Asn Gly Gly Val Gln Ser Gly Gly Leu Ile Lys
 50 55 60
 Asn Glu Ser Glu Leu Thr Gln Met Thr Ile Lys Gln Glu Thr Glu Gly
 65 70 75 80

Asn Ile Asn Glu Ala Arg Arg Glu Glu Asp Glu Glu Gln Asp Glu
85 90 95
Asp Ser Arg Thr Ser Met Pro Pro Ala Leu Gly Glu Asp Asp Asp Tyr
100 105 110
Glu Glu Asp Asp Ala Asp Ser Phe Ile Asp Lys Thr Asn Thr Pro Pro
115 120 125
Pro Ser Gln Ser Phe Leu Glu Gly Cys Arg Ala Ala Asn Leu Pro Asn
130 135 140
Asp Ile Val Thr Gly Ala Trp Glu Thr Tyr Asn His Ala Val Gln Arg
145 150 155 160
Val Ser Leu Glu Gly Ser Glu Ser Ala Trp Gln Leu Ser Ala Ile Tyr
165 170 175
Tyr Tyr Leu Leu Ser Lys Gly Ile Lys Arg Arg Gly Lys Thr Ile Arg
180 185 190
Ile Leu Ile Gln Pro Phe Pro Val Ser Ile Leu Thr Ile Ala Asn Ser
195 200 205
Phe Asp Ile Ser Val Ala Glu Met Leu Asp Lys Thr Ala Arg Phe Val
210 215 220
Glu Ile Ile His Ser Arg Lys Ile Arg Arg Tyr Gln Glu Tyr Ile Arg
225 230 235 240
Arg Ile Gln Glu Gly Leu Ala Val Ser Cys Val Ile Phe Lys Lys Phe
245 250 255
Cys Arg Ile Phe Cys Lys Ile Phe Glu Glu Ile Lys Val Gly Ser Glu
260 265 270
Asn Cys Pro Ser Ser His Glu Leu Phe Thr Val Leu Trp Thr Ser Phe
275 280 285
Leu Val Met Lys Ser Arg Met Thr Val Asp Asp Leu Ile Ser Asn Tyr
290 295 300
Gln Leu Leu Phe Ser Ile Leu Asp Gln Val Tyr Thr Glu Met Cys Ser
305 310 315 320
Met Lys Glu Gly Ile Val His His Leu Asn Gln Lys Phe Val Glu Asp
325 330 335
Leu Leu Glu Asn Asp Cys Thr Ile Ile Arg Ala Leu Cys Thr Gln Phe
340 345 350
Gly Gly Ser Val Leu Asp Ala Arg His Phe Ser Asp His Thr Phe Lys
355 360 365
Lys Met Glu Lys Thr Gly Ile Pro Ser Thr Trp Asn Phe Gln Glu Phe
370 375 380
Arg Asp Leu Ile Met Asn Val Pro Lys Thr Ala Tyr Glu Asn Tyr Leu
385 390 395 400
Leu Gln Arg Gly Ser Ile Asp Glu Arg Ile Phe Ile Pro Ser Val Glu
405 410 415
Asp Phe Ser Lys Ile Phe Gln Ser Pro Asp Thr Tyr Ser Val Ala Asp
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Ile Leu Lys Val Ser Tyr Ser Gly Arg Arg Phe Arg Asp Ala Glu Phe
435 440 445
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450 455 460
Gly Lys Val Ala Ser Glu Lys Leu Val Thr Gln Ser Lys Glu Gln Pro
465 470 475 480
Arg Val Pro Cys Val Glu Tyr Asn Leu Glu Leu Gly Asn Tyr Pro Asp

485 490 495
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 Ile Gly Ser Trp Lys Leu Glu Asn Ser Lys Leu Glu Glu Val Cys Gly
 515 520 525
 Thr Met Ser Asp Ser Pro Met Ala Thr Ile Leu Leu Lys Ser Asp Glu
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 Met Thr Asn Lys Phe Glu Arg Thr Leu Ser Ala Glu Leu Gly Glu Thr
 545 550 555 560
 Ile Asn Glu Asn Ile Pro Lys Tyr His Tyr Asn Val Arg Lys Glu Leu
 565 570 575
 Glu Leu Val Phe Leu Ile Phe Met Glu Lys Ile Ile Val Ala Glu Leu
 580 585 590
 Lys Lys Val Arg Glu Glu Asp Leu Leu Asn Val Ile Arg Arg Glu
 595 600 605
 Glu Phe Leu Asp Ser Val Phe Cys Phe Cys Val Glu Leu Ile Leu Val
 610 615 620
 Ser Asn Gly Tyr Asp Arg Pro Phe Pro Trp Ser Ala Glu Leu Cys Gly
 625 630 635 640
 Val His Pro Phe Met Phe His Lys Val Ile Asp Leu Met Ile Thr His
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 Glu Lys Gln Leu Ser Arg Gln Met Val Gln His Phe Ser Arg Ile Glu
 660 665 670
 Glu Thr Val Ile Glu Tyr Phe Ser Trp Lys Ser Asp Ser Pro Leu Trp
 675 680 685
 Pro Met Val Val Arg Cys Pro Phe Ala His Phe Gln Glu Phe Gly Glu
 690 695 700
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 Ile Lys Lys Pro Asp Asp Leu Arg Asp Glu Leu Gly Arg Pro Ile Val
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 Pro Gln Asn Gln Thr Ser Arg Thr Leu Arg Ile Phe Leu Lys Arg Thr
 740 745 750
 Tyr Phe Thr Ala Ala Arg Arg Leu Gln Asp Leu Thr Asp Arg Val Ser
 755 760 765
 Met Gly Ala Arg Ala Lys Ser Gln Cys Trp Ser Leu Phe Asp Tyr Leu
 770 775 780
 Leu Arg Asn Asp Thr Leu Ile Phe Met Asp Arg His Leu Asp Gln Ile
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 Leu Leu Cys Cys Val Phe Val Ile Met Lys Ile Asn Glu Ser Ser Met
 805 810 815
 Leu Phe Thr Glu Ile Met Ala Gln Tyr Arg Arg Gln Ser Ala Asn Ser
 820 825 830
 Leu Leu Val Tyr Arg Ser Val Thr Val Phe Gln Glu Gln Leu Asn Pro
 835 840 845
 Glu Asn Pro Gln Ala Val Asn Thr Lys Glu Thr Ile Leu Glu Arg Leu
 850 855 860
 Glu Gly Pro Gln Lys Glu Lys Thr Thr Val Asp Ile Ile Lys Tyr Tyr
 865 870 875 880
 Asn Ile Glu Phe Arg Asp Arg Ile Lys Tyr Ile Ile Gly Gln Ile Asp
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Ser Ala Ser Asp Glu Asp Leu Met Glu Met Pro Val Ala Thr Glu Ser
 900 905 910
 Gly Leu Met Pro Val Arg Val Tyr Leu Thr His Lys Leu Ser Ile Gln
 915 920 925
 Thr Leu Pro Lys Thr Lys His Gly Glu Ser Lys Gln Glu Arg Ala Ile
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 <212> DNA
 <213> Caenorhabditis elegans

<400> 4

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ccagcaaaac gaatcgactt agatataaag caagaattca atggtgagggt gcaaagtggaa	180
gggctgatta aaaatgaatc cgaattgact caaatgacaa tcaaacaaga aacagaagga	240
aacataaaatg aagcttagacg agaagaagaa gacgaagaac aagatgaaga ttccagaaca	300
tcaatgccac ctgcattggg agaagatgat gattatgagg aggatgatgc tgatagtttt	360
attgataaaa ctaatacacc gccaccatca caatcatttc tggaaaggatg tcgagcagct	420
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<212> PRT

<213> Caenorhabditis elegans

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35 40 45	
Asp Val Ala Lys Asp Asn Ser Asp His Thr Ile His Arg Leu Ile Leu	
50 55 60	
Gly Thr His Thr Ser Asp Glu Gln Asn His Leu Leu Ile Ser Lys Ile	
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Cys Met Pro Thr Asp Asp Ala Gln Phe Asp Ala Ser Arg Tyr Asp Thr	
85 90 95	
Glu Arg Ser Glu Tyr Gly Phe Gly Ala Val Asn Gly Lys Val Glu	
100 105 110	
Pro Asp Ile Arg Ile Asn His Glu Gly Glu Val Asn Arg Ala Arg Tyr	
115 120 125	
Met Pro Gln Lys Ser Asn Ile Ile Ala Thr Lys Ser Pro His Ala Asp	
130 135 140	
Val Tyr Ile Phe Asp Tyr Leu Lys His Ser Ala Val Pro Arg Asp Asn	
145 150 155 160	
Thr Phe Asn Pro Leu Ile Arg Leu Lys Gly His Thr Lys Glu Gly Tyr	
165 170 175	
Gly Leu Ser Trp Asn Pro Asn Lys Glu Gly Leu Ile Leu Ser Ala Ser	
180 185 190	

Asp Asp Gln Thr Val Cys His Trp Asp Ile Asn Ala Asn Gln Asn Val
 195 200 205
 Ala Gly Glu Leu Gln Ala Lys Asp Val Phe Lys Gly His Glu Ser Val
 210 215 220
 Val Glu Asp Val Ala Trp His Val Leu His Asp Gly Val Phe Gly Ser
 225 230 235 240
 Val Gly Asp Asp Lys Lys Leu Leu Ile Trp Asp Val Arg Thr Ser Thr
 245 250 255
 Pro Gly His Cys Ile Asp Ala His Ser Ala Glu Val Asn Cys Leu Ala
 260 265 270
 Phe Asn Pro Tyr Ser Glu Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys
 275 280 285
 Thr Val Ala Leu Trp Asp Leu Arg Asn Leu Arg Met Lys Leu His Ser
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 Phe Glu Ser His Arg Asp Glu Ile Phe Gln Val Gln Trp Ser Pro His
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 Asn Glu Thr Ile Leu Ala Ser Ser Gly Thr Asp Lys Arg Leu His Val
 325 330 335
 Trp Asp Leu Ser Lys Ile Gly Glu Asp Gln Ser Ala Glu Asp Ala Glu
 340 345 350
 Asp Gly Pro Pro Glu Leu Leu Phe Ile His Gly Gly His Thr Ala Lys
 355 360 365
 Ile Ser Asp Phe Ser Trp Asn Pro Asn Glu Pro Trp Val Val Cys Ser
 370 375 380
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 Gln


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 <212> DNA
 <213> Caenorhabditis elegans

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aacgagacta ttcttcgtat cagcggtact gataaacgtc ttcatgtgtg ggaccttatct	1020
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tacaacgaag ttgacgaaga aactccagcc gatgtggtag agagacaaca gtaaaatacg	1260
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<211> 575

<212> PRT

<213> *Caenorhabditis elegans*

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50	55	60	
Gly Leu Thr Asn Tyr Asn Glu Val Ala Asp Glu Leu Val Ala Asp Tyr			
65	70	75	80
Phe Gln Asn Asn Leu Ile Lys Gln Ile Asp Val Val Lys Gln Glu Tyr			
85	90	95	
Asp Met Lys Asn Ile Arg Arg Val Tyr Asp Ala Leu Asn Val Leu			
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Leu Ala Met Asn Ile Ile Thr Lys Ser Lys Lys Asp Ile Arg Trp Ile			
115	120	125	
Gly Leu Pro Ala Ser Ala Ser Gln Glu Ile Ser Arg Leu Glu Glu Glu			
130	135	140	
Lys Ser Arg Arg Glu Ala Ser Ile Ser Ser Lys Lys Gln Ala Leu Glu			
145	150	155	160
Glu Met Val Leu Gln Ile Val Ser Tyr Lys Asn Leu Val Glu Arg Asn			
165	170	175	
Arg Lys Asn Glu His Lys Asn Gly Arg Pro Glu Asn Asp Thr Val Leu			
180	185	190	
His Leu Pro Phe Leu Ile Ile Asn Thr Asp Lys Glu Ala Asn Val Glu			
195	200	205	
Cys Ser Val Ser Ser Asp Lys Ser Glu Phe Leu Phe Ser Phe Asp Lys			
210	215	220	
Lys Phe Glu Ile His Asp Asp Phe Glu Ile Leu Lys Lys Leu Asn Leu			
225	230	235	240
Ala Cys Ser Leu Glu Thr Thr Asn Pro Thr Ala Glu Glu Val Lys Thr			
245	250	255	
Ala Lys Ser Phe Leu Pro Thr Leu His Gln His Tyr Val Asp Glu Ile			

A7
WT

260 265 270
 Ile Ala Asn Arg Lys Lys Val Glu Ala Glu Lys Glu Glu Lys Arg Lys
 275 280 285
 Gln Gln Gln Leu Ile Ala Asp Gln Met Ser Met Asn Leu Ser Gln Ala
 290 295 300
 Gln Tyr Val Glu Pro Thr Ser Ser Leu Ala Gln Met Ser Tyr Ser Ser
 305 310 315 320
 Arg Phe Asn Arg Gln Leu Gln Glu His Leu Ile Asn Asp Gly Ser Glu
 325 330 335
 Asp Arg Ser Ala Ala Gly Ile Met Glu Arg Asp Tyr Asp Met Asp
 340 345 350
 Lys Asn Val Asn Gln Gly Ser Ala Ser Arg Gly Pro Met Tyr Asn Thr
 355 360 365
 Tyr Ser Pro Gln Lys Ile Arg Ala Gln Val Asn Thr Pro Leu Gln Val
 370 375 380
 Pro Pro Val Thr Lys Arg Tyr Tyr Val Gln Lys Thr Gln Gly Pro Met
 385 390 395 400
 Lys His Asp Met Thr Pro Val Val Arg Thr Val Asn Arg Pro Tyr Ser
 405 410 415
 Thr Val Pro Pro Asp Arg Arg Leu Ser Thr Gly Ala Thr Ser Val Asn
 420 425 430
 Ser Gly Pro Val Lys Tyr Tyr Val Pro Gln Gly His Gln Pro Met His
 435 440 445
 Gln Pro Val Gly Gln Arg Tyr Arg Val Arg Pro Gln Gln Pro Gln Met
 450 455 460
 Ser His Met Gly Gln Pro His Gln Val Gln Gln Arg Val Val Tyr Pro
 465 470 475 480
 Ala Gly Ser Ile Ser Gly His Gln Leu Gln Pro Gly Gln Arg Ile Val
 485 490 495
 Thr Gln Arg Ile Val Ala Pro Gly Gly Pro His Pro Pro Gly Thr Ile
 500 505 510
 Val Arg Lys Val Ile Arg Lys Ile Val Val Asn Asn Pro Lys Gln Ser
 515 520 525
 Pro Ala Gln Gln Val Ile Gln Lys Lys Met Met Glu Gln Asp Met Cys
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 565 570 575

<210> 8
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 <212> DNA
 <213> Caenorhabditis elegans

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 aaccaaccgg actcagacat ttttccacga aagtttgtga aaaggtgaaa gaaaaaggat 300

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35 40 45

Asp Lys Ser Leu Gly Leu Leu Ala Lys Arg Phe Ile Arg Met Ile Gln

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Tyr Ser Pro Tyr Gly Arg Cys Asp Leu Asn Thr Ala Ala Glu Ala Leu

65 70 75 80

Asn Val Arg Gln Lys Arg Arg Ile Tyr Asp Ile Thr Asn Val Leu Glu

85 90 95

Gly Ile Gly Leu Ile Glu Lys Arg Ser Lys Asn Met Ile Gln Trp Lys

100 105 110

Gly Gly Asp Phe Met Leu Asn Val Lys Glu Gly Lys Arg Leu Ser Ala

115 120 125

Thr Thr Glu Glu Asp Arg Met Glu Gln Leu Lys Ala Glu Ile Glu

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Gln Leu Asn Lys Glu Glu Leu Ile Glu Gln Arg Gln Arg Trp Leu
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 195 200 205
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 <213> Caenorhabditis elegans

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 <213> *Caenorhabditis elegans*

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 35 40 45
 Pro Glu Glu Ser Glu Pro Val Pro Met Lys Cys Leu Asp Phe Glu Glu
 50 55 60
 Ala Phe Gln Ser Glu Ser Val Ser Lys Gly Tyr Glu Ser Pro Tyr Lys
 65 70 75 80
 Asn Ile Ser Phe Leu Lys Glu Asp Ala Val Thr Val Asn Thr Met Ser
 85 90 95
 His Cys Pro Ala Asp Asp Ile Ala Lys Leu Ile Arg Asn Ile Gln Asn
 100 105 110
 Ser Val Tyr Thr Leu Gly Ile Glu Glu Ala Arg Gln Cys Arg Arg Gly
 115 120 125
 Lys Leu Leu Asn Val Leu Lys Pro Thr Gly Ser Ala Ser Pro Arg Tyr
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<213> *Caenorhabditis elegans*

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Glu Val Asn Gln Gly Leu Val Lys Asp Glu Pro Ile Asp Thr Ser Ser
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His Arg Val Tyr Val Pro Pro Pro Arg Pro Val Gln Arg Lys Leu Trp
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Lys Leu Phe Gln Pro Gly Pro Ser Thr Pro Gly Ser Ser Gln Tyr Thr
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Val Arg Asn Leu Ser Asn Leu Ser Gly Ser Pro Ser Met Tyr Asp Arg
115 120 125
Gln Pro Ala Ser Leu Pro Arg Thr Val Gln Pro Met Gly Leu Glu Met
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Gly Asn Ser Glu Gln Arg Lys Val Tyr Ile Asp Met Lys Asp His Val
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Ser His Ile Arg Leu Lys Thr Lys Lys Val Phe Ala Pro Gly Gln
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Arg Lys Pro Cys Asn Cys Thr Lys Ser Gln Cys Leu Lys Leu Tyr Cys
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Asp Cys Phe Ala Asn Gly Glu Phe Cys Arg Asp Cys Asn Cys Lys Asp
195 200 205
Cys His Asn Asn Ile Glu Tyr Asp Ser Gln Arg Ser Lys Ala Ile Arg
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Gln Ser Leu Glu Arg Asn Pro Asn Ala Phe Lys Pro Lys Ile Gly Ile
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Ala Arg Gly Gly Ile Thr Asp Ile Glu Arg Leu His Gln Lys Gly Cys
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Ala Lys Val Pro Cys Thr Asp Arg Cys Lys Cys Lys Gly Cys Gln Asn
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 <211> 3535
 <212> DNA
 <213> Homo sapiens

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<212> PRT

<213> Caenorhabditis elegans

<220>

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Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Cys Xaa Cys Xaa Xaa Cys

20 25 30

<210> 18

<211> 31

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<213> Caenorhabditis elegans

<220>

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20 25 30